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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/661,780

09/15/2003

Philippe Bouchard

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08/29/2006

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EXAMINER

KWON, BRIAN YONG S

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 08/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/661,780

Applicant(s)

BOUCHARD ET AL.

Examiner

Brian S. Kwon

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22,26-34 and 36-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☒ Claim(s) 22,26-34 and 36-42 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>01/23/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. By Amendment filed March 14, 2006, claims 22, 26, 28-34 and 36-42 have been amended.
2. Claims 22, 26-34 and 36-42 are currently pending for prosecution on the merits of the case.

Summary of Action

3. The objection of claim 39 is not maintained in light of the amendment/remarks filed March 14, 2006.
4. The rejection of claims 22, 26-34, 36-38 under 35 USC 112, second paragraph, is not maintained in light of the amendment/remarks filed March 14, 2006.
5. The rejection of claims 22, 26-34 and 36-42 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of USP 6,319,192 is not maintained in light of the approved Terminal Disclaimer filed March 14, 2006.
6. Applicant's arguments with respect to claims 22, 26-34 and 36-42 have been considered but are moot in view of the new ground(s) of rejection.

Priority

7. This application is a CIP of 08/786,937 01/22/1997, abandoned, which claims benefits of 60/011,282 filed 02/07/1996.

Although the concept of using LHRH-antagonist (e.g., ganirelix, anatarelax antide, azaline B, ramorelix, A-76154, Nal-Glu, 88-88 and cetorelix) for the treatment of infertility

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disorder was disclosed in above mentioned priority documents, the instantly claimed subject matter, which is drawn to a method of using LHRH-antagonist (e.g., ganirelix, anatarelax antide, azaline B, ramorelix, A-76154, Nal-Glu, 88-88 and cetorelix) in combination with hMG or recombinant FSH and clomiphene for the treatment of fertility disorder was not disclosed in the priority documents.

As discussed above, since the concept of using said LHRH-antagonist in combination with hMG or recombinant FSH and clomiphene was not disclosed until the instant filing date 09/15/2003, the instant invention is not entitled to have the earliest filing date of the priority documents.

Objection to Specification

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: “ovulation is induced by recombinant LH” in claim 33, “ovulation is induced by native LHRH” in claim 34, “native LHRH... is administered so that luteal phase supplementation is avoided...” in claim 37 and “recombinant LH, native LHRH or LHRH agonist...” in claims 34, 37 and 38 respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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9. Claims 22, 26-34 and 36-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for “treating female infertility”, does not reasonably provide enablement for “treating fertility disorder”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for treating fertility disorder by administering LHRH antagonist in combination with hMG or recombinant FSH and clomiphene.

The interpretation of the term “fertility disorder” (given “the reasonably broadest interpretation”) allows for the inclusion of various disorders that cause infertility of men and women including pelvic inflammatory disease, endometriosis, ovulation disorders, polycystic ovarian syndrome, abnormal cervical mucus, antiphospholipid syndrome in women and varicoceles, oligospermia, congenital absence of the Vas Deferans, Klinefelter’s syndrome, Young’s syndrome, Kartagener’s syndrome in men.

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The state of art recognizes the use of combination therapy, particularly the combination of LHRH-antagonist in combination with clomiphene or hMG or recombinant FSH (with or without induction of ovulation with HCG, native LHRH, LHRH-agonists or recombinant LH, or progesterone or alternatively combined with oral contraceptive preparation), for treating female infertility by improving ovarian stimulation in female patient (WO 00/59542; WO 99/55357; Hwang et al. "Human Reproduction, Vol. 18, No. 1, pp. 45-49, 2003; Nikolettos et al., European Journal of Obstetrics & Gynecology and Reproductive Biology, 97, 2001, pp. 202-207); Engel et al., Human Reproduction, Vol. 17, No. 8, pp. 2022-2026, 2002).

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the treatment of various fertility disorder by the administration of the instant combination therapy.

Similar to the prior art method, the instant specification discloses the administration of LHRH-antagonist (i.e., cetrorelix) in combination with clomiphene and hMG or recombinant FSH (with or without HCG) to treat female infertility (Examples 1-2). However, there is no demonstrated correlation that the tests and results apply to the treatment of "fertility disorder" embraced by the instant claims. Especially, there is no support or evidence that the claimed combination therapy would benefit male infertility disorder.

Since the efficacy of the claimed compound(s) in treating "fertility disorder" mentioned above cannot be predicted from a priori or the instant specification but must be determined from the case to case by painstaking experimental study and when the above factors are weighed

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together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 22, 26-34 and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 22 contains trademark or trade name such as A-76154, Nal-Glu, 88-88. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe certain LHRH-antagonists and, accordingly, the identification/description is indefinite.

In addition, dependent claim 37 recites the limitation "native LHRH " in claim 22. Furthermore dependent claim 38 recites the limitation " recombinant, native LHRH or LHRH agonist" in claim 22. There is insufficient antecedent basis for these limitations in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 22, 28-32, 36, 39-42 are rejected under 35 USC 102 (a) as being anticipated by Hwang et al. (Human Reproduction. Vol. 18, No. 1, pp. 45-49, 2003).

Hwang teaches the administration of LHRH antagonist such as cetrorelix and inducing follicle growth by the administration of hMG in combination with clomiphene for treatment of female infertility, wherein ovulation is induced by HCG; clomiphene is administered daily dosage of 100 mg from day 3 to 7 days; cetrorelix is administered as daily 2.5 s.c. injection started on 6th day of the ovarian stimulation followed by a multiple daily dose of 0.25mg injections (abstract; “Materials and Methods” in page 46; “Discussion” pages 48-49).

Although Hwang does not mention specifically about the activity of LHRH antagonist (i.e., cetrorelix) in “suppressing endogenous LH while maintaining FSH secretion at a natural level and estrogen development is not affected until ovulation induction” (claim 22) or “luteal phase supplementation is avoided and negative effects of HCG are prevented during the luteal phase” (claim 37), such property must be inherently presented in the referenced method. The prior art directing the administration of same compound in overlapping dosage to same patient population for the same intended purpose as disclosed by the applicant anticipates the applicant’s claim even absent explicit recitation of the mechanism of action.

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12. Claims 22, 26, 28 and 39-42 are rejected under 35 USC 102 (b) as being anticipated by Craft et al. (Human Reproduction. Vol. 14, No. 12, pp. 2959-2962, 1999).

Craft teaches the administration of LHRH antagonist such as cetrorelix and inducing follicle growth by the administration of human gonadotrophin in combination with clomiphene for the treatment of female infertility, wherein clomiphene is administered daily dosage of 100 mg from day 2 for 5 days; cetrorelix is administered as daily 0.25 mg s.c. injection started on the 5th or 6th day of gonadotrophin (abstract; “Drug Protocol” in page 2960 and “Discussion” in page 2961).

Although Craft does not mention specifically about the activity of LHRH antagonist (i.e., cetrorelix) in “suppressing endogenous LH while maintaining FSH secretion at a natural level and estrogen development is not affected until ovulation induction” (claim 22) or “after cessation of cetrorelix administration, subsequent follicle development is facilitated with remaining endogenous LH and FSH” (claim 39), such property must be inherently presented in the referenced method. The prior art directing the administration of the same compound in overlapping dosage to the same patient population for the same intended purpose as disclosed by the applicant anticipates the applicant’s claim even absent explicit recitation of the mechanism of action.

13. Claims 22, 27-28, 36-37 and 39-42 are rejected under 35 USC 102 (b) as being anticipated by Engel et al. (Human Reproduction. Vol. 17, No. 8, pp. 2022-2026, 2002).

Engel teaches the administration of LHRH antagonist such as cetrorelix and inducing follicle growth by the administration of human gonadotrophin or rFSH in combination with clomiphene for treatment of female infertility, wherein ovulation is induced by HCG;

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clomiphene is administered daily dosage of 100 mg from day 2 or 3 to 7 days (group 1) or 2 or 3 days to 5 days (group 2); cetrorelix is administered as daily 0.25mg s.c. injection started on 6th day of the ovarian stimulation (abstract; Figure 1; “Stimulation Protocols” in page 2023; “Discussion” in pages 2024-2025).

Although Engel does not mention specifically about the activity of LHRH antagonist (i.e., cetrorelix) in “suppressing endogenous LH while maintaining FSH secretion at a natural level and estrogen development is not affected until ovulation induction” (claim 22), “luteal phase supplementation is avoided and negative effects of HCG are prevented during the luteal phase” (claim 37) or “after cessation of cetrorelix administration, subsequent follicle development is facilitated with remaining endogenous LH and FSH” (claim 39), such property must be inherently presented in the referenced method. The prior art directing the administration of the same compound in overlapping dosage to the same patient population for the same intended purpose as disclosed by the applicant anticipates the applicant’s claim even absent explicit recitation of the mechanism of action.

14. Claims 22, 33-38 and 39 are rejected under 35 USC 102 (b) as being anticipated by Engel et al. (WO 99/55357).

Engel teaches the administration of LHRH antagonist such as cetrorelix and inducing follicle growth by the administration of human gonadotrophin or rFSH in combination with clomiphene for treatment of female infertility, wherein ovulation is induced by HCG, native LHRH, LHRH-agonists or recombinant LH (abstract; page 1, lines 24-33; page 3, lines 4-26; claims).

Although Engel does not mention specifically about the activity of LHRH antagonist (i.e., cetrorelix) in “suppressing endogenous LH while maintaining FSH secretion at a natural level and estrogen development is not affected until ovulation induction” (claim 22), “luteal phase supplementation is avoided and negative effects of HCG are prevented during the luteal phase” (claim 37), “ovarian hyperstimulation syndrome is avoided” (claim 38), or “after cessation of cetrorelix administration, subsequent follicle development is facilitated with remaining endogenous LH and FSH” (claim 39), such property must be inherently presented in the referenced method. The prior art directing the administration of the same compound in overlapping dosage to the same patient population for the same intended purpose as disclosed by the applicant anticipates the applicant’s claim even absent explicit recitation of the mechanism of action.

Conclusion

15. No Claim is allowed.
16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Patent Examiner
AU 1614

A handwritten signature in black ink, appearing to be 'BK' followed by a long horizontal stroke.